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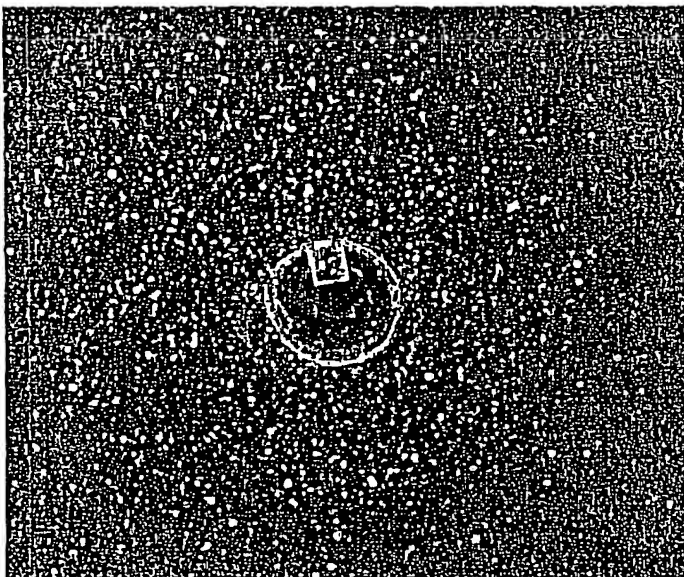
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(54) Title: METHOD FOR IDENTIFYING CELLULAR GROWTH INHIBITORS



(57) Abstract: The present invention is a method which permits the selective screening for growth-inhibiting substances having a known mechanism of action; i.e., substances which inhibit or otherwise interfere with an enzyme or other gene product whose function is required for the growth or survival of the cell. The method employs cells (e.g., bacterial cells) that contain a nucleic acid fragment that encodes an RNA fragment that can interfere with the expression of a gene product (e.g., an anti-sense RNA that hybridizes to a mRNA), wherein expression of the RNA fragment pre-sensitizes the cell to substances (drugs) that act at the gene product (e.g., a protein or RNA). The cells lose the capability to express the RNA fragment. In the method, the recombinant cells are grown in a nutrient medium in the presence of a test substance under conditions in which expression of the RNA fragment occurs at a level that pre-sensitizes the cell to substances that act at the targeted gene product. The growth conditions are also controlled such that the cells lose the capability to express the RNA

fragment. When the test substance is a growth inhibitor that acts on the targeted gene product, the cells lacking the RNA fragment (revertant cells) will have a growth advantage over cells containing the RNA fragment, and the growth of revertant cells will occur. The method of the invention includes monitoring the cell growth for the appearance of revertant cells, which leads to the identification of selective growth inhibitors having a specific mode of action.

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